



# Prescribing Guidelines for Pennsylvania



## TREATMENT OF ACUTE AND CHRONIC PAIN IN PATIENTS WITH SICKLE CELL DISEASE

**S**ickle cell disease (SCD) is the most common inherited blood disorder.<sup>1</sup> In the United States approximately 100,000 Americans have sickle cell disease. There are several different forms of SCD, with homozygous SCD (HbSS) and S $\beta$ 0 thalassemia being the most severe, accounting for about 70% of cases. Other forms include hemoglobin S $\beta$ + thalassemia and hemoglobin SC, which is usually

associated with milder symptoms. There are also some less common variants with different degrees of severity. HbS/hereditary persistence of fetal hemoglobin rarely causes symptoms due to the high level of fetal Hb. Sickle cell trait (HbAS) is a benign carrier state, not a chronic disease, but can become symptomatic under conditions of significant hypoxia.

Pain from SCD can present as acute, chronic, or a mixture of acute and chronic pain.<sup>2</sup> Recurrent episodes of acute, severe pain is common in patients with SCD. The acute pain experience associated with SCD is highly variable, both between patients and between episodes within the same patient. Acute pain episodes often occur spontaneously, but they can be caused by certain triggers such as other painful events, infection, dehydration, exposure to extreme and/or sudden changes in temperature and stress. While most acute episodes can be treated in the home setting, patients may seek pain care in the emergency department (ED) setting when the episodes are not responsive to home treatment and may require admission for further evaluation and pain control. Upon discharge, the patient should be referred to their primary care provider and/or to the outpatient prescriber of their pain medication.

It is important to note that SCD patients with acute painful crises often experience significant delays in receiving pain treatment,<sup>3</sup> and their pain is often inadequately treated.<sup>4</sup>

Patients with SCD may also develop chronic pain, which adversely impacts physical and mental functioning and overall quality of life. About 30% of adult patients with SCD report experiencing pain over 50% of the time.<sup>5</sup> It is important to note that repeated episodes of acute pain, which is commonplace in patients with SCD, can lead to the development of peripheral and central

nervous system sensitization, and adversely impact pain treatment efforts.<sup>6</sup> Some SCD patients may develop hyperalgesia, which can impact treatment of both acute and chronic pain states.<sup>7</sup> Many SCD patients often experience depression and anxiety. Chronic pain, recurrent episodes of acute pain, fatigue and negative encounters with medical professionals<sup>8,9</sup> may be contributing factors. Treatment of depression and anxiety through the use of medications, self-management programs and/or cognitive-behavioral therapy can improve symptom burden and may improve pain severity, frequency and duration.<sup>10</sup>

Multimodal pain care may lessen symptom burden in SCD patients experiencing chronic pain. One study suggests that long-term use of opioids for the treatment of chronic pain in patients with SCD is not associated with improved outcomes, as patient-reported pain intensity and physical functioning is often not improved.<sup>11</sup> However, long-term use of opioids for the treatment of chronic pain in patients with SCD has not been carefully studied. An assessment of the patient's response to treatment, including pain relief, side effects, and functional outcomes, should guide long-term use of opioids.<sup>12</sup>

These guidelines are intended to provide best practices related to the treatment of acute and chronic pain in patients with SCD. They are intended to help healthcare providers improve patient outcomes and to supplement, but not replace, the individual provider's

clinical judgment. It is recommended that providers review other evidence-based guidelines for Sickle Cell Disease, such as the National Institutes of Health 2014 Expert Panel Report: Evidence-Based Management of Sickle Cell Disease.<sup>12</sup> The American Society of Hematology has also released clinical practice guidelines for SCD and is currently in the progress of creating more<sup>13</sup>. The Pennsylvania State Guidelines related to the use of opioids to treat pain in a variety of patient populations and treatment settings provide insight into treatment options for other patient populations.

### *Acute Painful Crises*

1. Patients and their families should be educated on possible triggers and options to help decrease the frequency of acute painful crises and methods for immediate treatment when they occur. Patients and their family should be educated on when to seek further evaluation and treatment, often when oral analgesia has not been effective in controlling pain. This can include a process to receive timely care in the ED or an infusion center, or an established process to receive inpatient admission for further evaluation and treatment.<sup>14</sup>
2. Patients presenting with acute painful crises should be evaluated for possible common associated conditions, including infection, dehydration, hypovolemia, acute chest syndrome, severe anemia, cholecystitis, splenic enlargement, abdominal crisis and neurological events (including transient ischemic attack or stroke).<sup>1</sup>
3. When patients are presenting for care in the ED setting with severe pain, initial patient evaluation should be completed, and patients should receive pain treatment as quickly as possible.<sup>12</sup> In general, analgesic treatment should not be withheld pending lab work and/or detailed evaluation for common associated conditions.
4. Optimal outcomes may be achieved through the use of a standardized process in the ED for patient evaluation, rapid institution of pain therapy, and IV hydration. Patients should be triaged as a high priority.<sup>12</sup>
5. Scheduled acetaminophen should be continued or administered when not contra-indicated.
6. Scheduled non-steroidal anti-inflammatory drugs (NSAIDs) should be continued or administered when not contra-indicated.
7. Outpatient providers of patients with SCD should consider hydroxyurea treatment to decrease the frequency of acute painful crises. Hydroxyurea treatment improves survival in patients with SCD and decreases the number of acute painful crises experienced per year.

However, hydroxyurea treatment does not effectively treat existing pain.

8. Opioids are often necessary for the treatment of acute painful crises in SCD patients. Although opioids should be used in the lowest effective dose for the shortest duration possible, patients with acute painful crises may require aggressive initial opioid doses to achieve adequate pain control.
  - a. SCD patients should have an established protocol for the use of oral opioids in the home setting to lessen the frequency of ED visits or hospitalization. Individualized patient protocols should be used to help guide pain treatment in the ED and inpatient settings. This may reduce the need for long-term outpatient opioid use.<sup>15</sup> If a patient does not have a pain management plan for the home setting, they should be referred to their appropriate outpatient provider to establish one.
  - b. When presenting for acute painful crisis, patients should undergo rapid clinical assessment followed by pain treatment as quickly as possible.<sup>12</sup> When possible, institutions should establish a standard protocol that can

be individualized for patients to optimize patient outcomes.

- c. Pain care in the ED setting often is started with the use of IV opioids. When IV access is difficult, alternative routes should be considered. It is important to note that though there are situations when IV push opioid administration is necessary, there is growing concern that this delivery method may increase risk of opioid misuse, abuse, and addiction.<sup>23</sup>
- d. Patients requiring inpatient treatment may benefit from IV patient-controlled analgesia (IV PCA). IV PCA appears to be most effective when pain control is achieved first via IV bolus administration<sup>16-18</sup> (please see caution above). PCA should begin in the ED when possible and once admitted if not initiated in the ED.<sup>12</sup>
- e. Centrally acting sedatives, including benzodiazepines and Z-drugs, should not be administered concurrently with potent opioids. Patients should be educated on the risk of respiratory depression and potential death if both are combined.

- f. Short-term opioids may be necessary at the time of discharge.<sup>19</sup> However, upon discharge, the patient should be referred to their primary care provider and/or to the outpatient prescriber of their pain medication to evaluate the current opioid dosage and tapering plan.

### *Chronic pain care*

1. Patients with SCD who have chronic pain should undergo a comprehensive evaluation for the underlying cause(s) of the pain. The evaluation may need to be completed by a pain specialist in collaboration with the patient's hematologist and/or primary care provider.
  - a. The evaluation should be comprehensive and include an assessment of pain, mood (including an assessment for depression and anxiety), sleep and physical functioning.
2. Chronic pain care should be interdisciplinary in nature and include use of non-opioid medications and techniques such as physical therapy, cognitive behavioral therapy, deep tissue/deep pressure massage therapy, muscle relaxation therapy, osteopathic manipulative therapy and self-hypnosis as indicated.
3. Evaluation and treatment by a pain psychologist may be helpful for educating patients on proper self-management techniques for chronic pain.<sup>20,21</sup>
4. Clinicians should be mindful of intrinsic biases that may be contributing to racial disparities in pain management for patients with sickle cell disease. Clinicians should also use caution to avoid stigmatizing language in the medical chart as this may contribute further to biases in treatment.
5. Occupational therapy can have a direct therapeutic impact on the physiological structures and psychosocial experiences that cause pain by modifying postures, positions, or activities that cause stress; designing custom orthotics or adaptive equipment to improve participation; and implementing sensory strategies and mind-body connection techniques to decrease the impact of acute anxiety and other psychosocial comorbidities of pain.
6. There is growing concern that the use of chronic opioids in patients with SCD may not improve pain outcomes. Patients with SCD who have developed hyperalgesia may not benefit from long-term use of opioids and the use of long-term opioids, especially at high daily doses, may worsen it. When starting chronic opioid therapy, the clinician should discuss the risks and potential benefits associated with

treatment, so that the patient can make an informed decision regarding treatment. Reasonable goals and expectations for treatment should be agreed upon, and the patient should understand the process for how the care will be provided.

- a. Patients receiving long-term opioid therapy should be cared for in accordance with established clinical treatment guidelines on the use of opioids for the treatment of chronic noncancer pain in patients with SCD.<sup>12</sup>

- i. In patients who have engaged in aberrant drug-related behaviors, clinicians should carefully determine if the risks associated with long-term opioid therapy outweigh document benefit. Clinicians should consider restructuring therapy (frequency or intensity of monitoring), referral for assistance in management, or discontinuation of long-term opioid therapy. Appropriate referral for substance use disorder evaluation and treatment should be provided. A clinician may refer the patient

to their insurance carrier or the Department of Drug and Alcohol Programs Get Help Line at 1-800-662-4357 (HELP) or [www.DDAP.PA.GOV](http://www.DDAP.PA.GOV).

- b. Patients who would like to taper off long-term opioid therapy should speak with their provider to develop an individualized tapering plan. Patients with SCD undergoing an opioid taper are likely to require a slow taper over an extended period of time.
    - i. Providers should review the risks and benefits of the current therapy with the patient and check the patient's Prescription Drug Monitoring Program (PDMP), as required by Act 191 of 2014, to help determine if tapering of opioids is appropriate based on individual circumstances. Providers can review the Health and Human Services Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics for further guidance.<sup>22</sup>

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